

REMARKS

Applicants respectfully request reconsideration of the present application.

CLAIMS STATUS

Applicants have cancelled claims 3, 5, 7, 17 and 19-21 without prejudice or disclaimer. Applicants reserve a right to file one or more continuation applications directed to the cancelled subject matter.

Applicants have amended claims 1, 2, 4, 6, 8-16, 18 and 22-23 without prejudice or disclaimer. Support for the amended claim 1 may be found throughout the application as filed and more specifically on page 12, line 25, through page 13, line 5. No new matter has been added. Applicants reserve a right to file one or more continuation applications directed to the subject matter omitted by the present amendment in one or more continuation applications.

After the amendment, pending claims include examined claims 1, 2, 4, 6, 8-16, 18 and 22-23 and withdrawn claims 24-26.

Applicants thank the Examiner for the June 12th interview.

ELECTION/RESTRICTIONS

On October 19, 2006, in a telephone conversation with Alexey Sapargin (Reg. # 56,439), the Examiner requested Applicants to elect a single invention among the following groups:

- I. Beta lactams having T = S or SO. Claims 2, 15-18 and 20-21 and embodiments of claims 1, 4-14, 19 and 22-23 with T = S or SO.
- II. Beta lactams having T = O. Claim 3 and embodiments of claims 1, 4-14, 19 and 22-23 with T = O.
- III. Starting materials of claims 24-26.

During a telephone conversation on October 24, 2006, between Alexey Saprinin and the Examiner, Applicants made a provisional election with traverse of Group I, claims 1-2, 4-23 for prosecution on the merits. In the present communication, Applicants affirm the October 24th election. Applicants respectfully submit that at least the intermediate III and the product I have unity of invention, the standard for restriction in a national phase entry application like this.

REJECTION FOR IMPROPER MARKUSH GROUP

Claims 1, 2-14, 19 and 22-23 stand rejected as drawn to an improper Markush Group. Applicants believe that the present amendment obviates the rejection. The subject matter of Group II may or may not be pursued in a divisional application.

CLAIMS OBJECTIONS

The PTO objects to 6 and 10-18 for informalities detailed on pages 9-10 of the March 22nd Office Action. Applicants believe that the present amendment obviates the objection.

CLAIMS REJECTION UNDER 35 U.S.C. § 112, ¶ 2

Claims 1-2, 4-23 stand rejected as indefinite. Applicants believe that the revised claims obviate the rejection.

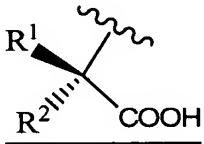
CLAIMS REJECTION UNDER 35 U.S.C. §112, ¶ 1

Claims 1-9, 15, 19-20 and 20-23 stand rejected as failing to comply with the enablement requirement. Applicants believe that the present amendment obviates the rejection.

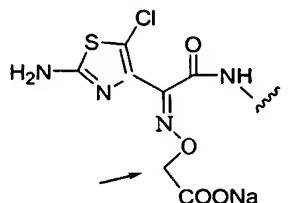
CLAIMS REJECTIONS UNDER 35 U.S.C. § 102

Claims 1, 2, 4-5,7-8, 10, 15, 20 and 22-23 stand rejected as anticipated by Nishimura, Journal of Antibiotics, Vol. 45, 1992, p. 485-499. Applicants traverse.

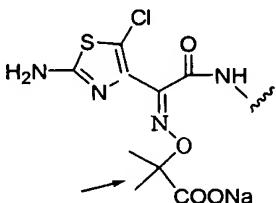
Nishimura does not teach at least one element recited in the pending claims. For example, Nishimura does not teach A-COOH having the formula:



wherein R¹ is hydrogen and R² is lower alkyl as the amended claims require. Applicants submit that compounds 10 and 11 of Nishimura are outside of the scope of the amended claims. For the Examiner's convenience, Applicants provide formulae of Nishimura's compounds 10 and 11 below:



compound 10

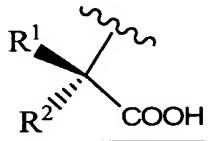


compound 11

As Nishimura does not teach all the elements of the claimed invention, Applicants request withdrawal of the rejection.

Claims 1, 2, 4-5, 7-8, 10, 15, 20 and 22-23 stand rejected as anticipated by Miyake (US patent no. 4,788,185). Applicants traverse.

Miyake does not teach at least one element of the claimed invention. For example, Miyake does not teach A-COOH having the formula:

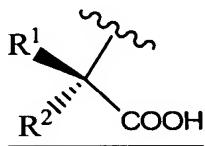


wherein R¹ is hydrogen and R² is lower alkyl as the amended claims require. Applicants submit that each of compounds from the examples 92, 108, 109, 110 (column 128, lines 3-15), 111-112 and 113 have the same R¹ and R² the same using Applicants' terminology, quite

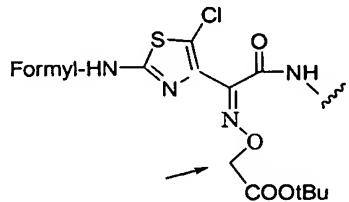
in contrast to the claimed invention. As Miyake does not teach all the elements of the claimed invention, Applicants request withdrawal of the rejection.

Claims 1, 2, 4-5, 7-8, 10-11, 15, 20 and 22-23 stand rejected as anticipated by Kawabata (WO97/41128). Applicants traverse.

Kawabata does not teach at least one element of the claimed invention. For example, Kawabata does not teach A-COOH having the formula:



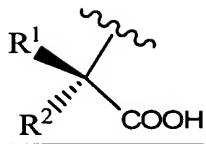
wherein R¹ is hydrogen and R² is lower alkyl as the amended claims require. For the Examiner's convenience, Applicants provide the formula of the compound from the example 14 of Kawabata.



Applicants further submit that in Kawabata's compound from the Example 14, using Applicants' terminology, R¹ and R² are both H; in Kawabata's compound from Example 16, R¹ and R² are both methyl; in Kawabata's compound from Example 39, R¹ and R² are both H; in Kawabata's compound from Example 48, R¹ and R² are both H; in Kawabata's compound from Example 49, R¹ and R² are both methyl. In conclusion, as Kawabata does not teach all the elements of the claimed invention, Applicants request withdrawal of the rejection.

Claims 1, 2, 4-5, 7-8, 10-13, 15-17 and 22-23 stand rejected as anticipated by Takaya (US patent No. 4,427,677). Applicants respectfully traverse.

Takaya does not teach at least one element of the claimed invention. For example, Takaya does not teach A-COOH having the formula:



wherein R¹ is hydrogen and R² is lower alkyl as the amended claims require. Applicants respectfully submit that in the compound of Example 2 in Takaya, using Applicants' terminology, R¹ and R² are both H; in the species 4 of Example 3 in Takaya, R¹ and R² are both H; in the species 5 of Example 3 in Takaya, R¹ and R² are both H; in the species 1 of Example 5 in Takaya, R¹ and R² are both H; in the species 3 of Example 5 in Takaya, R¹ and R² are both H; in the compound of Example 6 in Takaya, R¹ and R² are both H. In sum, as Takaya does not teach all the elements of the claimed invention, Applicants respectfully request withdrawal of the rejection.

CLAIMS REJECTIONS UNDER 35 U.S.C. §103

Claims 6 and 9 stand rejected as obvious over Nishimura, Journal of Antibiotics, Vol. 45, 1992, p. 485-499. Applicants respectfully traverse.

The PTO base its case of obviousness on close structural similarity between the compounds 10 and 11 of Nishimura and the claimed compounds.

In response, Applicants respectfully submit that the claimed compounds possess unexpectedly superior antibacterial properties compared to their homologues, such as compounds 10 and 11 of Nishimura. In support, Applicants submit a declaration under 37 C.F.R. § 1.132 of Dr. Yoshinori Yamano, which presents comparison of antibacterial activity for nine series of compounds. Each of the nine series included three compounds labeled A, B and C. More specifically, nine different Z⁺ groups were used for compounds A, B and C to produce the (9×3)=27 different compounds tested. Within each of the nine series, the compound labeled A is a compound of formula (I) as defined in claim 1 of the present application, with T=S, X=Cl, R² = methyl, R¹ = hydrogen; the compound labeled B has R² = hydrogen, but otherwise is identical to the corresponding compound labeled A; the compound labeled C has R¹ = methyl, but otherwise is identical to the corresponding compound labeled

A. Thus, with each of the nine series, compounds B and C are homologues of their respective compound A, which differ from the compound A by the absence or the presence of methyl group in the A group of formula (I) respectively. Compounds A from each series are within the scope of the amended claim 1, while compounds B and C from each series are outside the scope of the amended claim 1.

Based on results of the tests, Dr. Yamano concluded that

- 1) Each of compounds A demonstrated an overall inhibitory activity against a broad spectrum of bacterial strains unexpectedly superior to that of its respective compounds B and C. The difference in the overall inhibitory activity against the broad spectrum of bacterial strains of compounds A on one hand and either of their respective compounds B and C on the other hand is statistically significant, see Dr. Yamano's declaration, page 7.
- 2) Each of compounds A had the inhibitory activity against cephem resistant bacterial strains 8) *E. cloacae* RS4321(Bla++), 10) *P. aeruginosa* SR24-12 (Bla+) and 14) *H. influenzae* SR11435(BLNAR) unexpectedly superior to that of its respective compound B, while the inhibitory activity against cephem sensitive bacterial strains 5) *E. coli* NIHJ JC-2, 7) *E. cloacae* ATCC 13047, and 9) *P. aeruginosa* SR24 of compounds A and their respective compounds B was similar, see Dr. Yamano's declaration, page 7.
- 3) Each of compounds A had the inhibitory activity against cephem sensitive bacterial strains 5) *E. coli* NIHJ JC-2, 7) *E. cloacae* ATCC 13047, and 9) *P. aeruginosa* SR24 unexpectedly superior to that of its respective compound C, while the inhibitory activity against cephem resistant bacterial strains 8) *E. cloacae* RS4321(Bla++), 10) *P. aeruginosa* SR24-12 (Bla+) and 14) *H. influenzae* SR11435(BLNAR) of compounds A and their respective compounds C was similar, see Dr. Yamano's declaration, page 7.

Applicants respectfully submit that compounds 10 and 11 of Nishimura are compounds 1-B and 1-C of Dr. Yamano's declaration.

In sum, as the claimed compounds demonstrate unexpectedly superior antibacterial properties compared to their homologues differing in the absence or presence of methyl in the A-group of formula (I), Applicants respectfully request withdrawal of the rejection.

Claims 6 and 9 stand rejected as obvious over US patent no. 4,788,185. Applicants respectfully traverse.

The PTO based its case of obviousness on close structural similarity between compounds recited in the '185 and the claimed compounds.

Applicants refer the PTO to the discussed above Dr. Yamano's declaration that demonstrated the claimed compounds have unexpectedly superior antibacterial properties compared to their homologues differing in the absence or presence of methyl in the A-group of formula (I) and accordingly request withdrawal of the rejection.

Claims 1, 2, 4-5, 7-8, 10-13, 15-17, 20 and 22-23 stand rejected as obvious over US patent no. 4,559,102. Applicants respectfully traverse.

Applicants respectfully submit that the '102 patent does not teach or suggest at least one element of claim 1. In particular, the '102 patent does not teach or suggest the compound



of formula (1) with A-COOH having the formula: $R^2 \cdots \text{COOH}$, wherein R^1 is hydrogen and R^2 is lower alkyl. Because the '102 patent does not teach all the elements of the claimed invention, no *prima facie* obviousness is established. Thus, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe that the present application is in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By Stephen B. Maebius

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicants
Registration No. 35,264